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TITLE: Clinical Study of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for Severe Pelvic Fracture & Intra-Abdominal Hemorrhagic Shock using Continuous Vital Signs

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14. ABSTRACT

Hemorrhage remains a leading cause of death in military trauma settings. Reports from the battlefield have found that over 50%
of potentially salvageable deaths are related to uncontrolled non compressible torso hemorrhage (NCTH). Severe pelvic injury
with associated junctional femoral hemorrhage results in hemorrhagic shock. Endovascular techniques such as intra-aortic
balloon occlusion have the potential to significantly decrease blood loss, improve physiologic parameters, and ultimately lead to
increased survival in patients in hemorrhagic shock from severe pelvic injury.

15. SUBJECT TERMS

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Introduction

Hemorrhage remains a leading cause of death in military trauma settings. Reports from the battlefield have found that over 50% of potentially survivable deaths are related to uncontrolled non-compressible torso hemorrhage (NCTH). This sustained burden of NCTH morbidity and mortality from the current conflict has led to the recognition of the imperative need to develop better methods and devices to manage vascular disruption, hemorrhage and hemorrhagic shock.

Profound hemorrhagic shock can occur after traumatic high amputations with associated junctional femoral hemorrhage, severe pelvic injury, and intraabdominal vascular injury with the most common mechanism being improvised explosive device (IED) blast. Current treatment options include blood product resuscitation, the use of anti-fibrinolytic medication (TXA), pelvic binder stabilization, junctional tourniquets, open pre-peritoneal pelvic packing (PPP), open aortic cross-clamping, and angiographic embolization. However, these therapies have proven to be logistically difficult to employ in the forward setting and have been only moderately successful in the prevention of exsanguination from NCTH. Thoracotomy with aortic cross-clamping in the face of exsanguination in the emergency room has a survival rate of 7%. Thoracotomy for a similar purpose prior to abdominal exploration has not been studied extensively, but reported survival rates range from 1-42%. In addition to poor survival rates, open ligation of pelvic hemorrhage is time consuming, requires a fully equipped operating room and surgical staff and results in high morbidity due to an open incision and pelvic ischemia. The option of transarterial embolization is generally not available at forward surgical sites.

Resuscitative balloon occlusion of the aorta (REBOA) has been clinically demonstrated to stop bleeding below the diaphragm. It has the potential to significantly decrease blood loss thereby decreasing blood-product resuscitation requirements, improve physiologic parameters, and ultimately lead to increased survival in patients in hemorrhagic shock from severe torso injury. This is a simple endovascular technique which can be taught to forward deployed physicians and has over the past decade vastly improved the survival of ruptured abdominal aortic aneurysm patients. Although the technique is still in its infancy for trauma patients, we predict that the use of intra-aortic balloon occlusion will improve the survival of trauma patients and reduce morbidity.

The use of endovascular technology in the treatment of injury has steadily increased over the past 2 decades. In conjunction with increased use, a decrease in morbidity and mortality has been observed in certain patient populations. The outcomes from ruptured abdominal aortic aneurysms have significantly improved due to the use of the intra-aortic occlusion balloon to minimize hemorrhage, improve hemodynamic stability, and provide adequate time for operative preparation and planning.

The intra-aortic occlusive balloon placed through an open approach was first described for controlling major aortic hemorrhage in the Korean War. Since that time, it has been used percutaneously in many clinical disciplines as an effective and minimally invasive means of achieving rapid proximal control of hemorrhage. Reports of use for control of bleeding during pelvic surgery, hepatobiliary surgery, orthopedic surgery, postpartum hemorrhage, and repair of ruptured AAA (Abdominal aortic aneurysm) suggest that the intra-aortic occlusion balloon is a life-saving measure. Physiologic parameters such as serum lactate, pH, pCO_2, and central, cerebral and coronary perfusion in animal models of hemorrhagic shock have been shown to improve with intra-aortic balloon occlusion.

Preliminary evidence on the use of resuscitative endovascular balloon occlusion of the aorta (REBOA) for trauma has been published [19-21] and indications for the procedure include control of non-compressible torso hemorrhage in the abdomen and pelvis. The first published algorithm for the use of REBOA was developed by our institution (Figure 1). The indications include refractory hypotension due to severe pelvic and/or intra-abdominal injury. Locations for balloon occlusion have been described. Stannard et, al. published a technical description of REBOA in which aortic occlusion zones were defined in order to facilitate a better understanding of the technique and to provide a framework with which to study and refine its use. Zone I is the descending thoracic aorta between the origins of the left subclavian and celiac arteries. Zone I REBOA is akin to thoracic aortic clamping otherwise performed during resuscitative thoracotomy. Zone II is the paravisceral segment and was proposed as a potential no-occlusion zone, while Zone III represents the infra-renal aorta extending from the lowest renal artery to the aortic bifurcation. Despite the anatomic plausibility of Stannard's technical description, it is not a clinical report, simply an anatomic recommendation based on zones of aortic perfusion.

The rationale behind REBOA follows the understanding that temporary aortic occlusion supports life sustaining myocardial and cerebral perfusion until a time when resuscitation can be initiated and surgical hemostasis obtained. These are exactly the goals of open thoracic aortic cross clamping, but REBOA can potentially improve survival by avoiding the morbidity of the rapidly performed thoracotomy and cross clamping.

Due to the improvements in mortality seen in the past 2 decades with the use of aortic balloon occlusion for ruptured AAAs, it is reasonable to apply the technique in the setting of trauma. Furthermore, the dismal outcomes from emergent thoracotomy and aortic cross-clamping demand a better approach to NCTH. It stands to reason that REBOA may be able to increase survival; however, the techniques of the procedure and clinical use require investigation.

Continuous Vital Signs and Shock Index

The need to adequately interpret vital signs trends and subsequently respond rapidly to resuscitative needs is paramount following trauma. Large quantities of real-time patient monitoring data are now available through hospital vital signs monitoring systems, yet vital signs are typically recorded manually periodically by clinical staff. Non-invasive continuous vital signs monitoring provides accurate real-time displays of hemodynamic and perfusion data that might allow for superior detection of circulatory deficits that can contribute to both significant organ dysfunction and death. Continuous monitoring may both allow early recognition of pathologic processes which require intervention and may give clinicians feedback on the pathophysiological processes present in the patient before and after intervention. The use of continuous data collection allows linear, episodic data to be converted to 2-dimensional analysis. Previous research at Shock Trauma has led to the two-dimensional representation of shock index (SI = heart rate (HR)/ systolic blood pressure (SBP) as a method of visualizing the hemodynamic status of patients. In figure 2, a two dimensional representation of shock index over time is shown for patients in hemorrhagic shock. Patient A recovered, while patient B's shock index spiraled downwards to the right over time.

Our goal is to apply this sophisticated data collection tool in order to provide real time data regarding the physiologic consequences of REBOA. By capturing heart rate, heart rate variability, pulse oximetry, temperature, end tidal CO2, respiratory rate, systolic blood pressure and MAP (if arterial line present) on REBOA patients, we will be able to quantify the physiologic changes associated with REBOA in a linear fashion as they relate to time and length of balloon occlusion, systolic blood pressure and MAP.

The continuous vital signs monitoring should demonstrate the rapidity with which hemodynamic stability occurs after balloon inflation, the degree of stability, and the physiologic changes associated with balloon deflation. Such detailed data will allow further honing of our techniques and protocols. In addition to the real-time, time-stamped continuous vital signs data, all trauma bays and operating rooms at STC are recorded by video cameras from multiple angles, which gives us the ability to thoroughly document the exact time course of resuscitation efforts.

Simulation:

Virtual reality simulation training (VRS) is a well-established means of skill development in many industries including aviation and military operations [23]. The use of simulated models to train surgeons for specific skills has become a major modality of modern training. Simulation appears to lead to improvements in medical knowledge, comfort in procedures, and improved performance during re-testing in simulated scenarios [24-26]. The use of VRS in medicine has increased exponentially, with training modules and formally endorsed courses available in laparoscopy, endoscopy, anesthesia, trauma, interventional radiology, interventional cardiology, and vascular surgery. Only a few studies have shown improvements in clinical outcomes as a result of simulation training, [27, 28] but evidence suggests that trauma surgery skills and outcomes may be improved with simulator training. Advantages to using VRS include automated objective assessment and haptic feedback, no radiation exposure, no patient harm, and the ability to document and store progress for each user over time.

In the mid-1970s, the use of simulation for clinical skills training first gained currency with the introduction of Advanced Cardiac Life Support (ACLS) and ATLS training. [33-36] A randomized study found that surgical residents and attending faculty with simulator training had greater proficiency in suturing, transferring, and mesh placement than the control group. [37] When tested in an *in vivo* pig model, surgeons randomized to the simulator training arm were more proficient in these same skills. [38] Surgical residents randomized to a video-trainer versus no formal training over a 30 day period do uniformly better on pre-specified tasks. [39] Residents trained on laparoscopic surgery simulators show improved procedural performance in the operating room, and residents trained on simulators are more likely to adhere to advanced cardiac life support (ACLS) protocols than those who receive standard training. [40-41] As noted above, questions about the validity of simulator training for surgery reflect the lack of good data about what really happens in the process of doing these procedures. What data there are tends to focus on team, not individual, clinical performance. However, there is no consensus on the objective analysis of technical performance by clinicians. [42] There are no standard methods of evaluation for surgical performance, nor is there agreement on how such metrics might improve clinical outcomes. [43]

Study Overview

We have undertaken a 2 phase study to evaluate simulation-based REBOA training and the effectiveness of REBOA stabilization of severe intra-abdominal hemorrhagic shock and/or

pelvic fracture patients. In phase I, a simulator based REBOA training curriculum was developed to train STC clinicians, and its efficacy will be evaluated. Phase 2 is a single center, 2 year prospective observational study in which 150 patients with severe hemorrhagic shock and/or pelvic fracture admitted to the Trauma Resuscitation Unit of our level 1 trauma center are stabilized with REBOA. The physiological status of the patient was monitored continuously via continuous vital signs monitoring. Our main objective was to assess the impact on mortality and morbidity after REBOA. We have 2 hypotheses and 7 associated specific aims. We hypothesized that use of REBOA in cases of NCTH will decrease morbidity and mortality associated with this often fatal pattern of injury.

Keywords

Trauma
Hemorrhage
Junctional Hemorrhage
Non-Compressible Torso Hemorrhage (NCTH)
Combat Casualty Care
Aortic Occlusion
REBOA
Resuscitative Endovascular Occlusion of the Aorta
Thoracotomy
Aortic cross-clamp
Simulation
Virtual reality simulation
Endovascular

Accomplishments

Specific Aim 1: Design and evaluate a comprehensive simulator based training program to train attending trauma surgeons, critical care faculty, trauma fellows, and chief residents to perform REBOA.

Task 0 (Complete): Obtain Institutional Review Board approval from both UMD and MRMC IRB board. See Appendix

Task 1 (Complete): REBOA skills training and standardization of procedure

Specific Aim 2: Standardize clinical performance of REBOA using simulator and formalized standard operating procedures (SOP).

Task 2 (Complete): Standardize clinical performance of REBOA using simulator and formalized SOP (2-5 m).

2a. Standardize clinical performance of REBOA on simulator.

2b. Formalize standard operating procedures.

Milestones: Formal SOP written. (Complete)

SOP now includes catheter approved for use through 7Fr sheath.

Task 3 (Incomplete): Evaluate 30 physicians performance in REBOA placement in humans. (3-12 m).

3a. (Complete) Log simulator usage by each physician (3-12 m).

- ***43 of 30 physicians have performed as of 5/30/2016.***

3b. (Incomplete) Track physician performance in REBOA placement.

3c. (Complete) Interim analysis after first 15 physicians complete the course.

3d. Statistical Analysis.

Milestone: A validated REBOA placement training program. 90% complete

Task 4 (Complete): Obtain appropriate Institutional Review Board IRB approvals for retrospective and prospective human research and initiate study.

4a. Obtain both University of Maryland (UMD) and MRMC IRB approval for both retrospective review of all patients treated via REBOA at STC and for prospective enrollment of future patients who receive REBOA placement**.**

4b.-Train clinical staff - CORE research core and physicians in study. (Months 3-6)

4c. Develop study database. (3-6 m)

Task 5 (Complete): 30 patient Retrospective observational trial of REBOA (4-12m)

5a. For every REBOA placed between February 2013 to time of IRB approval at STC, perform chart review, obtain trauma registry pulls, and match continuous vital signs data to patient. Expected enrollment = 30 patients (4-12 m).

Final Retrospective Enrollment ending on 7/16/2015 – 33 patients

5b. Interim analyses based on total enrolled patients. Treatment efficacy assessed and SOP revised as necessary.

Task 6 (Ongoing): 24 patient Prospective observational trial of REBOA. (4-12 m).

6a. Place REBOA in approximately 24 patients with severe intra-abdominal hemorrhagic shock and/or pelvic fracture (4-12 m).

6b. Interim analyses every 20 patients enrolled to assess treatment efficacy and revise SOP as needed.

Task 6 (Ongoing): Clinical data analysis and interpretation.

6a. Statistical Analysis of outcomes, vital signs, and other patient information (10-12 m)

6b. Final reports and peer reviewed publications.

Milestones: Final reports and peer reviewed publications. (20-24 m).

- *Pending study completion*

Task 7 (Complete): Finalize Standard operating procedures for training and clinical use of REBOA. (10-12 m).

7a. Revise and finalize simulator training curriculum and guidelines with regards to study conclusions.

7b. Revise and finalize standard operating procedures and clinical practice guidelines

4. Impact

Impact/Outcomes Statement

Hemorrhage remains the leading cause of death in civilian trauma patients. Current therapies in the treatment of non-compressible torso hemorrhage (NCTH) include blood product resuscitation, the use of anti-fibrinolytic medication (TXA), pelvic binder stabilization, junctional tourniquets, open pre-peritoneal pelvic packing (PPP), open aortic cross-clamping, and angiographic embolization. However, these therapies are only moderately successful in the prevention of exsanguination from NCTH. Thoracotomy with aortic cross-clamping in the face of exsanguination in the emergency room has a survival rate of 7%. The use of the REBOA has the potential to contribute a life-saving measure in the treatment of NCTH by providing a more timely and less invasive intervention. The procedure can be utilized at major trauma centers to stabilize patients before definitive control of bleeding through either further operative or radiologic intervention.

Our goal is to provide not only the military with an accurate "natural history" of the physiologic effects of REBOA on humans, but also the civilian trauma and pre-hospital community as well. Once REBOA's effects and their time course are understood, forward triage decisions can be adjusted accordingly for patients who successfully receive this adjunct. Furthermore, in rural, austere environments where rapid transport may be unavailable, the benefit of REBOA is more pronounced as it allows temporization of NCTH to allow adequate resuscitation and transport to definitive care, accordingly. However, little is known about the effect of REBOA on humans in a clinical environment. Our study has contributed to the understanding of the procedure's effects in the short term, what patient populations may safely receive a REBOA, what patients may benefit the most. More study is needed, and as we continue to accrue patients, we can further elucidate answers to these questions: driving the deployment of REBOA to the patients that will benefit the most and in the proper setting.

Further, this procedure is straightforward and similar to other vascular access techniques and could easily be taught to physicians or physician extenders with experience in standard vascular access procedures. Recently, the need for prehospital deployment of this device has been advocated in the literature. The enthusiasm for field deployment has led to the development of purpose-built devices that could be used in the pre-hospital setting. One of these devices received recent regulatory approval for human use in the US. This raises the possibility of the device being utilized in a rural setting to stabilize patients with torso hemorrhage for immediate transport to a trauma center. The information gained from this research will allow not only the temporization of NCTH in rural areas or in the setting of delayed transport, but will also provide data on the most effective training strategies for all medical personnel, including pre-hospital providers and non-surgeons. Thus, our research will benefit civilian pre-hospital providers in the same ways as their military counterparts.

5. Changes/Problems

1. On November 9th, 2015, the University of Maryland transitioned their clinical electronic medical record to a new software package. This transition was anticipated, but our new electronic data tool had IT compatibility issues with the new software and was non-functional. Our backup procedures for paper documentation were re-initiated and continue currently.

2. The new electronic medical record, which necessitated a redesign of our electronic data tool. This is now complete and being used to enter and store study data.

3. Our CORE staff had unforeseen staffing issues on Thanksgiving Day 2015 and as a result, approximately 24 hours of prospective data collection time were lost. This did not affect our study as no patients matched screening criteria during this time.

4. Due to the riots during spring 2015, the city was closed to travel by all non-essential personnel. Our research staff was unable to report for work, resulting in a gap of 48 hours of prospective data collection. The clinical staff present in the Trauma Center assumed the responsibility of noting any REBOA placements. No placement occurred during this time and no data was lost.

5. On January 1, 2016, a newly FDA-approved device compatible with a smaller 7Fr sheath was available for clinical use. The SOP and data tool were updated in anticipation of these devices becoming available and were updated immediately. A total of 5 deployments occurred before the end of the first year of study.

6. Products

Descriptive Characteristics of Population (as of 10/1/2016)

		n	Mean ± SD
Total Patients		75	
Race	Black	38	
	White	33	
Gender	Male	64	
	Female	10	
Mechanism	Penetrating	23	
	Blunt	39	
ISS			38 ± 17
SBP			72 ± 55
HR			73 ± 50
GCS			6 ± 5
Mortality	Yes	54	
	No	19	

Brief Clinical Summary (Year 1)

During the initial year study period, 60 patients had REBOA for severe non-compressible hemorrhage and traumatic arrest. Mean age was 40±18 years. Mean admission GCS was 6±5 and median ISS 36±16. Mean admission SBP and HR was 98±52 and 104±47, respectively for those patients with vital signs. The distal thoracic aorta (Zone 1) was occluded in 76.7% of patients and 100% of those in arrest. 23.3% had distal abdominal aortic occlusion (Zone 3). Mean time to aortic occlusion (including cannulation) was 9.5±4.8mins and femoral artery cannulation was 3.6±1.6mins. Percutaneous access was used in 36%, and groin cutdown used in 64%, including 70% of those in arrest. Overall mortality was 77%, which included 59% for hemorrhage patients, and 93% for those in arrest. Of the patients arriving in arrest, 45% were resuscitated and went to the operating room. One patient required femoral bifurcation reconstruction, and two balloon ruptures occurred without sequelae after REBOA use. No aortoiliac injury, ischemia, or limb loss occurred from REBOA use.

See Appendix C for full data

NOTE: The above table represents the total experience of the study as of the date of submission of revised annual report. Totals here and in Appendix B may not be additive to 100% given ongoing data collection, partial data collection, and submission of abstracts at various time points.

Manuscripts

DoD Combat Casualty Care Research Program 2016 Supplement to Journal of Shock

1. Resuscitative Balloon Occlusion of the Aorta: Pushing care forward
   Authorship: W Teeter MD, A Romagnoli MD, J Glaser MD, A Fisher PA, J Pasley DO, B Scheele DO, M Hoehn MD, M Brenner MD

Abstracts

1th Annual Academic Surgical Congress Abstract Submission - February 2-4, 2016 in Jacksonville, FL

2. Virtual Reality Simulation for Residents: A Trainee Experience in Damage Control Endovascular Skills
   Authorship: William A. Teeter, MD, MS; Megan Brenner, MD, MS; Melanie Hoehn, MD; Deborah Stein, MD, MPH; Thomas Scalea, MD

39th Annual CONFERENCE ON SHOCK – June 11-14th, Austin, TX

3. REBOA IMPROVES MEAN BLOOD PRESSURE (MBP) AND SHOCK INDEX (SI) AS MEASURED BY CONTINUOUS VITAL SIGNS (CVS) EVEN IN PATIENTS ARRIVING IN ARREST
   Authorship: W Teeter MD, M Brenner MD, M Hoehn MD, P Hu PhD, S Yang PhD

75th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery - September 14-17, 2016, Waikoloa, HI

4. Time to aortic occlusion: It's all about access
   Authorship: A Romagnoli MD, W Teeter MD, J Pasley DO, P Hu PhD, G Hagegeorge, D Stein MD, T Scalea MD, M Brenner MD

5. Age is just a number: REBOA can be performed in older patients at high risk for atherosclerotic vascular disease
   Authorship: M Ghneim MD, W Teeter MD, A Romagnoli MD, M Hoehn MD, P Hu PhD, T Scalea MD, M Brenner MD

American College of Surgeons Clinical Congress 2016 - October 16–20, 2016, Washington, DC.

6. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) Can Be Deployed Rapidly and Safely by Acute Care Surgeons
   Authorship: D HAMPTON MD, W TEETER MD, G HAGEGEORGE, M HOEHN MD, D STEIN MD, T SCALEA MD, M BRENNER MD

7. Paradigm shift in hemorrhagic traumatic arrest: REBOA is at least as effective as RTACC
   Authorship: W Teeter MD, A Romagnoli MD, H Li PhD, S Yang PhD, P Hu PhD, D Stein MD, T Scalea MD, M Brenner MD

American College of Emergency Physicians Annual Meeting 2016, October 15-20th, 2016, Las Vegas, Nevada.

8. REBOA improves quality of resuscitation versus thoracotomy in patients in traumatic arrest.
   Authorship: William Teeter, MD MS, Anna Romagnoli, MD,, Melanie Hoehn, MD, Jay Menaker, MD, Deborah Stein, MD MPH, Thomas Scalea MD, Megan Brenner MD MS.

9. Virtual Reality Simulation can help prepare Emergency Medicine physicians for REBOA
   Authorship: W. Teeter MD, A Romagnoli MD, M Hoehn MD, J Menaker MD, D Stein MD, T Scalea MD, M Brenner MD

10. Participants & Other Collaborating Organizations

Organization: *University of Maryland, Baltimore – Shock Trauma & Anesthesiology Research Organized Research Center (STA-ORC)*

Name: *Megan Brenner*
Project Role: *PI*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.18*
Contribution to Project: *Supervise and contribute to study design, manuscript revision, and data analysis.*

Name: *Thomas Scalea*
Project Role: *PI*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.01994*
Contribution to Project: *Dr. Scalea met with all other PIs and Co-Investigators to discussed clinical research logistics, data management and results.*

Name: *Fu M. Hu*
Project Role: *Co-In*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.294*
Contribution to Project: *Integrating the data collection system for this study. He also works in the development and analysis of the continuous VS and in working with Dr. Brenner to design the join prediction models.*
Name: *Hegang Chen*
Project Role: *Statistician*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.05*
Contribution to Project: *The design, analysis and interpretation of the data.*

Name: *Jennifer Kidd*
Project Role: *Epidemiological Assistant I*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.55*
Contribution to Project: *Assist the project coordinator with patient identification, data abstraction, audit and collection, follow up and reporting.*

Name: *Raymond Fang*
Project Role: *Co-In*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.15*
Contribution to Project: *Provides experience as health care providers for military severe pelvic fracture and intra-abdominal hemorrhagic shock victims to maximize the military relevance of the results and their interpretation*

Name: *Catriona Miller*
Project Role: *Co-In*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.15*
Contribution to Project: Assists with the study design, study coordination and reporting, data collection, data storage, and data analysis.

Name: *Melanie Hoehn*
Project Role: *Co-Investigator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.037*
Contribution to Project: *Supervise and contribute to study design, manuscript revision, and data analysis.*

Name: *Christine Wade*
Project Role: *Manager, Clinical Research*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.50*
Contribution to Project: *She is responsible for overseeing the 24/7 coverage for the CORE Research Group.*

Name: *Eric Lund*
Project Role: *It Appt Int Engineer*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.05*
Contribution to Project: *He was responsible for overseeing the 24/7 basis obtain pre-hospital and admit data on every admit to the STC.*

Name: *Shiming Yang*
Project Role: *Research Associate*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.60*
Contribution to Project: Working Dr. Hu in the *acquisition, integrating, testing, and maintaining the trauma training center VS data collection system.*

Name: *Hsiao-Chi Li*
Project Role: *Graduate Research Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1.0*
Contribution to Project: Assisting Dr. Hu with development and analysis of the continuous VS and other project data analysis.

Name: *Umang Shah*
Project Role: *General Associate*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *0.15*
Contribution to Project: Research assistant who screens and obtains pre-hospital and admit data on admissions in STC.

Name: *George Hagegeorge*
Project Role: *IT Support Associate*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.60*
Contribution to Project: Assisting in the acquisition, integrating, testing and maintaining the trauma training center VS and video data.

Name: *Keven Barnes*
Project Role: *Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.20*
Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Name: *Diandra Browne*
Project Role: *Research coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.50*
Contribution to Project: IRB task management, IT design and assist with reporting.
.
Name: *Ryne C. Jenkins*
Project Role: *Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.20*
Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Name: *Rajan Patel*
Project Role: *Graduate Research Assistant*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *1.0*
Contribution to Project: To matching the patient vital signs with the REBOA procedure time and duration based on the video review. Assist in calculating the VS features for the study.

Name: *Ashley Hargrove*
Project Role: *Res Asst, Clinical*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.33*
Contribution to Project: Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Name: *Brandon Bonds*
Project Role: *Post-doc Fellow*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.25*
Contribution to Project: Assisting in the integration, testing, and maintaining the trauma training center VS data collection system.

Name: *Hannah Huber*
Project Role: *Res Asst, Clinical*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.55*
Contribution to Project: The coordination of activities between patient identification, data collection, follow up and reporting.

Name: *Seeta Kallam*
Project Role: *Res Project Coordinator*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.025*
Contribution to Project: IRB preparation, submission, maintenance, and compliance.

Name: *Anthony Herrera*
Project Role: *Res Acct, Clinical*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *.025*
Contribution to Project: Assist the project coordinator with patient identification, data collection, follow up and reporting.

Organization: University of Maryland Medical Center
Name: *William Teeter*
Project Role: *Research Resident*
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: *2.25*
Contribution to Project: Data management and QA review related to simulator training and clinical performance of REBOA.

11. Special Reporting Requirements

Nothing to Report

9. Appendices

Appendix A: Review of Data Capture Process: Continuous Vital Signs (VS) and Videography

Hypothesis 2:

Use of resuscitative endovascular balloon occlusion of the aorta (REBOA) in cases of non-compressible torso hemorrhage (NCTH) of the abdomen and pelvis will decrease the morbidity and mortality associated with this often fatal pattern of injury with improved physiological parameters, outcomes, and recovery periods and will allow time for vascular repair.

Technical Objectives and Associated Specific Aims:

1.) Evaluate the ability of REBOA to improve survival and functional outcomes in patients with NCTH. Analysis of continuously recorded vital sign data will show that the use of REBOA will improve physiologic parameters in patients with NCTH.

Real-time Continuous Vital Signs and video recording and archiving system

The need to adequately interpret vitals trends and subsequently respond rapidly to patient physiology and resuscitative needs is particularly paramount following trauma. Large quantities of real-time patient monitoring data are now available through hospital vital signs monitoring systems, yet vital signs are typically recorded manually periodically by clinical staff. Non-invasive continuous vital signs monitoring provides accurate real-time displays of continuous hemodynamic and perfusion data and trends that might provide for early detection of circulatory deficits that can contribute to both significant organ dysfunction and death. Continuous monitoring may both allow early recognition of pathologic processes which require intervention and may give clinicians feedback on the pathophysiological processes present in the patient before and after intervention.

Our goal is to apply this sophisticated data collection tool in order to provide real time data regarding the physiologic consequences of REBOA. By capturing heart rate, heart rate variability, pulse oximetry, temperature, end tidal CO2, respiratory rate, and systolic blood pressure and MAP (if arterial line present) on REBOA patients, we will be able to quantify the physiologic changes associated with REBOA in a linear fashion as they relate to time and length of balloon occlusion rate, and systolic blood pressure and MAP (if arterial line present).

Theoretically, the continuous monitoring of patient vital signs during balloon inflation should allow for assessment of time to hemodynamic stability, the degree of stability, and what happens to the patient physiologically when the balloon is deflated. Such detailed data will allow us to fine tune and perfect our technique. In addition to the real time, time stamped continuous vital

signs data, all trauma bays and operating rooms at STC are recorded by video cameras from multiple angles, which gives us the ability to thoroughly document the exact time course of resuscitation efforts.

Continuous vital signs collection:

Real-time patient VS data feed is collected (Bed Master) every 2 seconds and recorded for future analysis. Raw real-time VS waveforms, trends, and alarms are compressed more than 90%, transferred to a centralized VSDR server through the secure hospital intranet, and stored securely for linkage with demographic, injury-specific clinical, imaging, and general laboratory data for subsequent analysis. VSDR collects over 80 VS variables from conventional vital signs and physiologic parameters—SpO2, etc., shock index (systolic blood pressure divided by heart rate), continuous electrocardiogram, oxygen saturation, and end-tidal carbon dioxide waveforms at 240 Hz. The numerical values of heart rate, blood pressure, intracranial pressure, cerebral perfusion pressure, respiratory rate, and temperature, are recorded every 2 seconds. Data rates after compression averaged 76.4 KB/h for numerical and 12.3MB/h for waveforms. The VSDR server is interfaced with the Shock Trauma Research Registry, which provides patient demographic, admission assessment, laboratory, and outcome data. Custom processing and viewing programs, previously developed by our team, are used for real-time patient data abstraction, artifact removal, 5- to 60-minute time-window averaging, VS variability, and summary data output to both computer automatic processing and human reviewing.

The use of continuous data collection allows linear, episodic data to be converted to 2-dimentional analysis. Our goal is to apply this sophisticated data collection tool in order to provide data regarding the physiologic consequences of REBOA. By capturing heart rate, heart rate variability, pulse oximetry, temperature, end tidal CO2, respiratory rate, and systolic blood pressure and MAP (if arterial line present) on REBOA patients, we will be able to quantify the physiologic changes associated with REBOA in a linear fashion as they relate to time and length of balloon occlusion. The work proposed here will be based on 5, 10, 15, 30, and 60 minute-mean and standard deviations of the every-6-second raw data over the course of the balloon inflation. We will calculate the dose of time spent above and below certain vital sign thresholds or cut offs and record the minimum and maximal values. Vital signs before, during, and after REBOA placement will be assessed and compared. The stability of vital signs readings during REBOA placement will be compared to patient outcomes.

Triple redundant VS collection system and real-time Monitor of monitors for ensuring reliable data collection

In order to capture all the unscheduled and emergency REBOA cases, it is critical to develop a real-time patient vital signs collection network which will **capture all patient VS at anytime, anywhere** (13 TRU and 10 ORs).

STC has implemented a single VS collection server-based VSDR system in the past 10 years. The effective real-time data collection rate is between 60% to 80% for all 13 TRU and 10 ORs. The missing VS data collection was mainly due to hardware and software failure and no real-time notification of collection failure and user errors.

To ensure anytime, anywhere reliability (>99% collection rate) of real-time VS data collection, we designed and implemented a **triple redundant VS** collection system and real-time **Monitor of monitors (MoMs)** for live VS collection status notification.

Fig. 1 illustrates the triple redundant VSDR and MoMs system architecture.

BM1, 2, 3 are the VS trend data collection server and BMA,B,C are the waveform (240Hz) and alarm status collection server. All triple-redundant data servers including 3 vital signs trend data collectors (blue dots in Fig 1) and 3 waveform collectors (green dots in Fig 1), send the latest data with timestamps to the MoMs Sever. Fig. 2 shows a snippet of the MoMs system. Each data server is represented by a large block (Fig 2). Each bed unit collected by such server is represented by a colored small box. If a bed unit is online in the last 5 minutes, the box shows in green, with the admission status (admitted or discharged) and the last heart rate value. If a bed unit is offline for longer than 5 minutes, the box is colored as yellow. It turns red, if the bed unit has been offline longer than 6 hours.

Vital signs data of each one minute median are submitted to three independent MoMs servers (red dots). The MoMs server processes the data and provides the patient VS data collection status in real-time to any remote MoM viewer inside the hospital intranet (for security purposes).

With the implementations of the above system we have been able to improve our data collection rate to >99% for all patient beds.

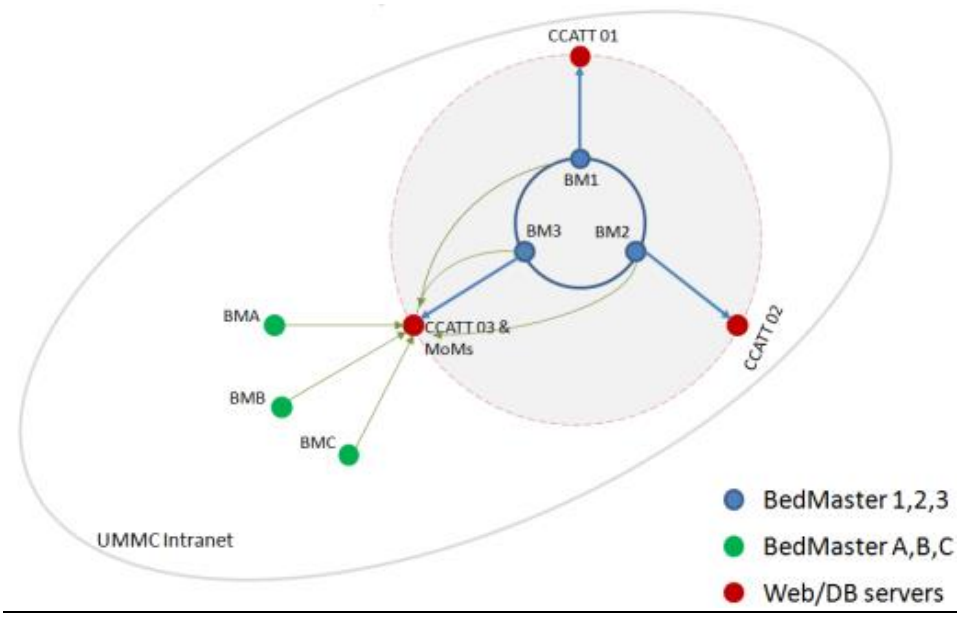


Fig. 1 Illustration of VSDR and MoMs system architecture

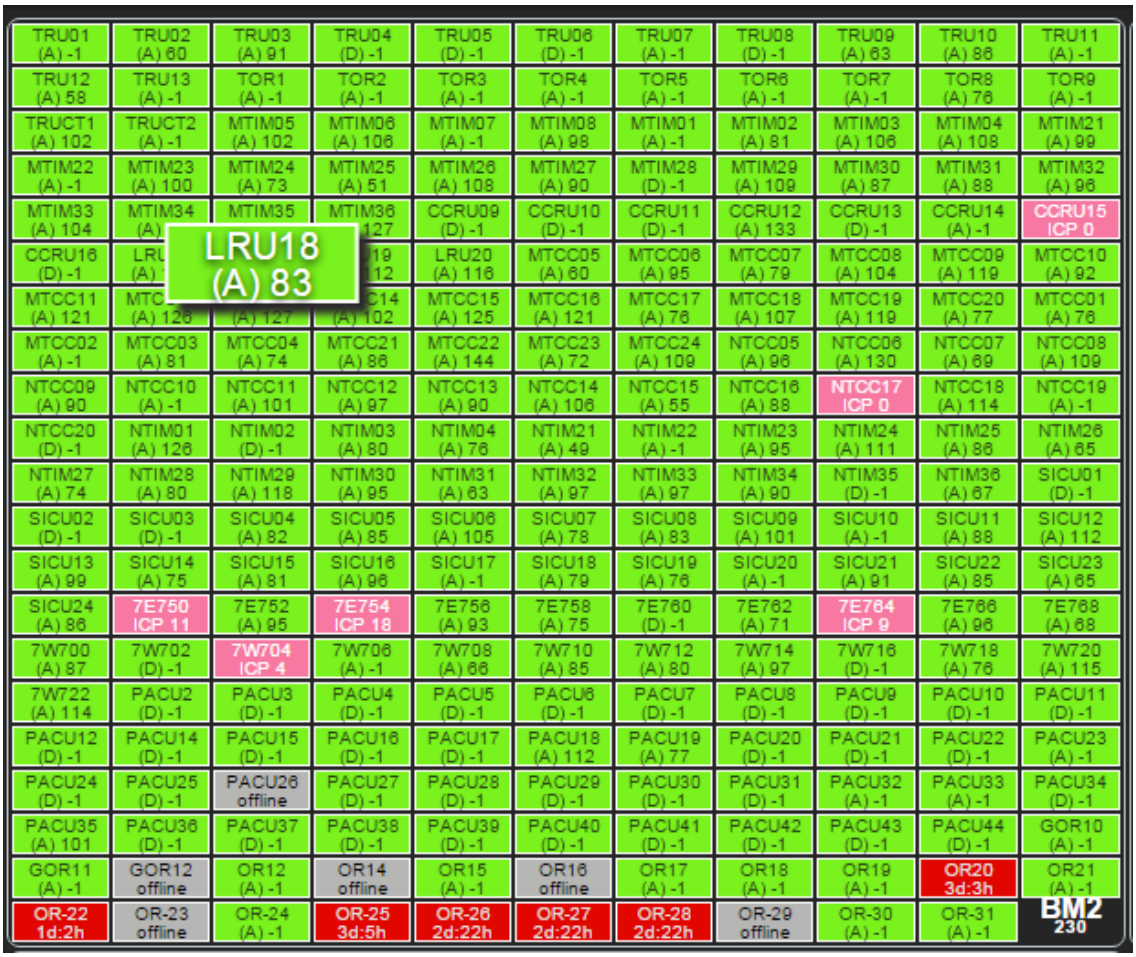


Fig. 2 A snippet of MoMs system of 230 bed units in one data server

Vital Signs data abstraction software.

The Vital Signs data abstraction software was developed to accurately match the vital signs for feature abstraction and statistical analysis. Based on the REBOA patient admission and insertion time (abstracted from videography), we are able to match vital signs data to REBOA performance metrics and aortic occlusion time with high accuracy.

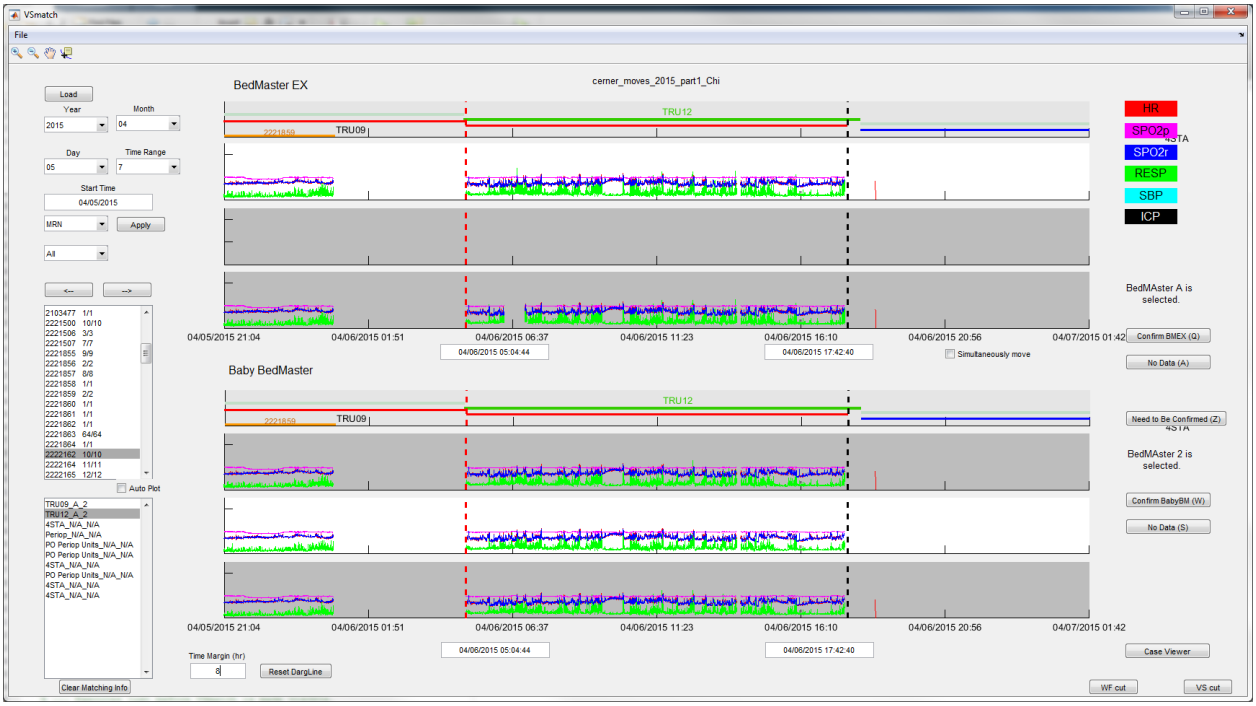


Figure 3. Vital Sign Matching Software

REBOA Vital Signs Viewer

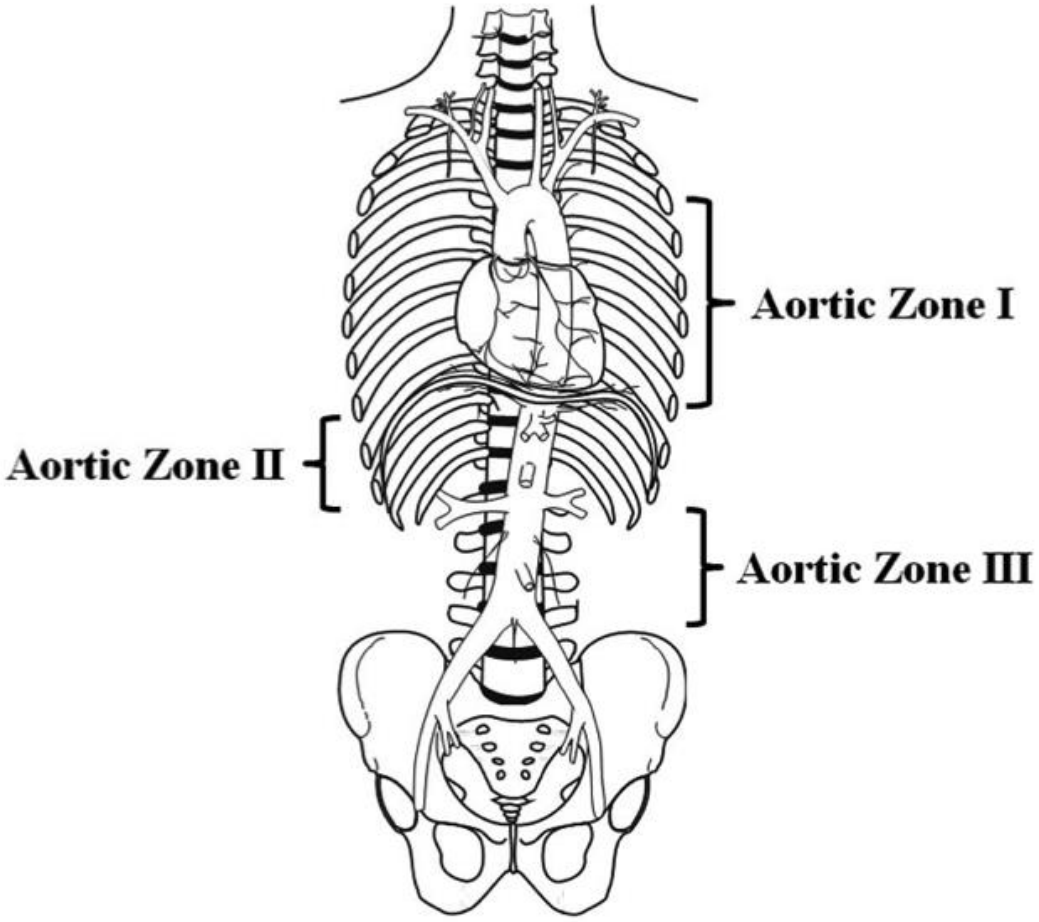
The REBOA Vital Signs Viewer was developed to provide the detailed evaluation of the physiological changes pre and post REBOA procedure.

Figure 4. REBOA case viewer

VS feature abstraction and statistical analysis.

A Total 36 cases are included in the current analysis out of 45 enrolled. Patients missing from this analysis are from the early retrospective period and continuous vital signs could not be matched with total accuracy. For the sake of data quality, our research group determined that they should be excluded from this portion of the analysis. All patient enrolled in 2014 were accurately captured. There are 7 female (19.4%) patients. They are all adult patients (age≥18 years), with average age of 44.1 years. Continuous vital signs with 0.5 Hz sample rate were collected for REBOA cases. Given recorded and videography-verified aortic occlusion time, vital signs of 5, 10, 15 minutes before and after the operation time were summarized into mean, median, dose. Based on the location of REBOA inflation (Zone 1 is at the diaphragm and Zone 3 just proximal to the iliac bifurcation **[See illustration below])** and presence vs absence of pulse on arrival to the TRU, the study cases are grouped into three categories:

1. Group 1 are patients with REBOA performed in Zone 1 with CPR (N=16)
2. Group 2 are patients with REBOA performed in Zone 1 without CPR (N=10)
3. Group 3 are patients with REBOA performed in Zone 3 (N=10).



We used the VS medians as a robust statistics to represent each case's physiological condition during peri-procedural time periods of 5, 10, and 15 minutes. In an initial exploration, we found that in general, systolic blood pressure (SBP), pulse pressure (PP), heart rate (HR), shock index (SI), EtCO2, SpHb were improved in the first 5, 10, or 15 minutes after the AO (aortic occlusion) compared to VSs in the same time range before AO. Figure 5 show the group mean of SBP, MBP, PP for before (blue bar) and after (red bar) AO in the 3 time ranges for the Group 1.

We used the one-side Wilcoxon signed-rank test to compare the paired samples from before and after AO. We consider p values from 0.05 to 0.1 as weak evidence, 0.01 to 0.05 moderate, and <0.01 strong evidence. In Group 2, SBP, MBP, PP, and SI all had improvement in a statistical significant sense ($p < 0.05$).

With the box-plot, we visualized the distribution of the median VSs for each group before and after AO time. Figure 6 shows the 5 minutes range. For example, in the Group 2, the median SBP has been increased after the AO, with higher median, higher 1^{st} and 3^{rd} quartiles, and narrower inter-quartile. This pattern is also seen in MBP, and PP. However, the SI, on the other hand, was seen to decrease after the AO, with all lower statistics, representing a positive change in patient physiology.

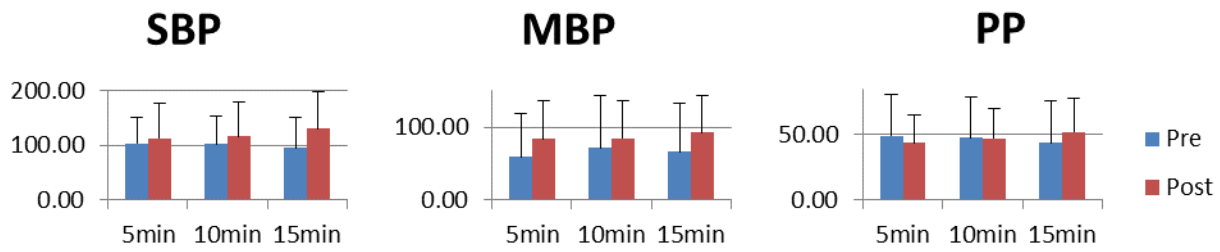


Figure 5. Average VSs for 5, 10, 15 minutes before (blue) and after (red) AO time in Group 1.

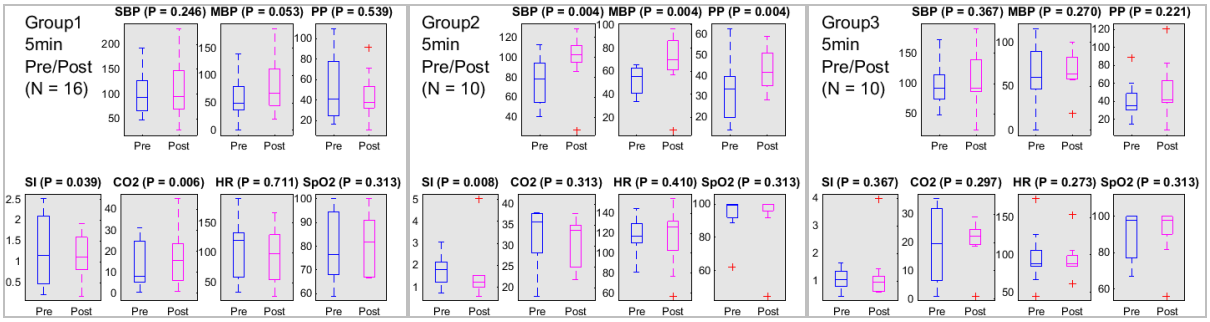


Figure 6. Box-plots for the 3 groups, comparing 5 minutes before (blue) and after (red) AO time. P-values are based on the Wilcoxon sign-rank test.

Realtime Video Recording System Infrastructure and Video Review:

The trauma bays in the STC TRU (trauma resuscitation unit) and the operating rooms have integrated audio-visual recording capability and are recorded continuously from multiple angles. This video capability will allow us to obtain exact timelines of REBOA placement and other resuscitation efforts during REBOA placement as necessary to ensure accuracy. Video is stored for 48 hours prior to being deleted without appropriate IRB approvals.

The TRU bays are video recorded by three cameras pointed toward the patient resuscitation area at each bay. The camera over the lower extremity of the patient is the Axis P5534 Pan/Tilt/Zoom IP camera. The camera behind the head area of the patient and also the camera located outside the bay are fixed position Axis P3344-6MM.

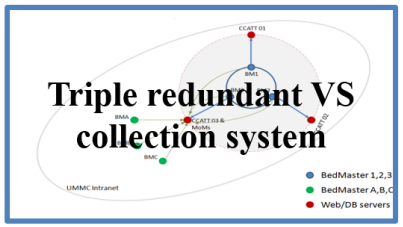
Capture of all video signals (including other patient care units) are distributed across five HP PowerEdge R310 servers, Intel Xeon 2.27GHz processors with 4 GB RAM running an embedded version of Windows. Videos are rendered via Vision Client 7.2.1 and output in AVI format utilizing H.264/MPEG-4 AVC video codec for playback on common media players.

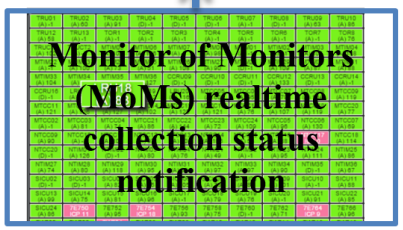
Prospective REBOA Data Collection and Analysis

Real-time VS data collection

VS & Video Data Processing

REBOA Case Analysis





VS Case matching And REBOA VS Viewer

VS Feature abstraction

Real-time patient status collection (STC-CORE)

Shock Trauma Registry ISS, Age, GCS etc

Statistic Analysis/ Modeling and Report

Video recording

24X7 Video recording for 13 TRU and 10 OR

Video Review

Timing of REBOA and Events

Appendix B: Narrative for Hypothesis 1

Narrative for Hypothesis 1, Tasks 1-3.

Task 1: REBOA skills training and standardization of procedure (0-2 Month (m)).

Task1a. Standardize REBOA technique. *Milestones: Standardized protocol for REBOA placement.* (0-2 m).

(Complete) A standardized protocol for REBOA placement was established. The common femoral artery is accessed either directly via open cut-down or percutaneously using external landmarks only or using ultrasound guided placement. Once accessed, dilators are then utilized to upsize to the appropriate sized sheath (12 Fr sheath if using CODA® catheter (Cook Medical, Bloomington, IN), and 7 Fr sheath if using ER-REBOA™ (Prytime Medical, Boerne, TX)). Catheter insertion distance is then approximated using external morphometric landmarks. The catheter system (including wire for CODA® catheter) is then inserted to the appropriate distance. Radiographic confirmation of catheter placement is suggested prior to balloon inflation (although blind balloon inflation has been performed without complication during this study). The balloon should then be inflated and additional radiographic confirmation should be obtained.

Task 1b. Develop VIST simulator training program with powerpoint lectures and hands-on training. *Milestones: VIST simulator training program curriculum (0-2 m).*

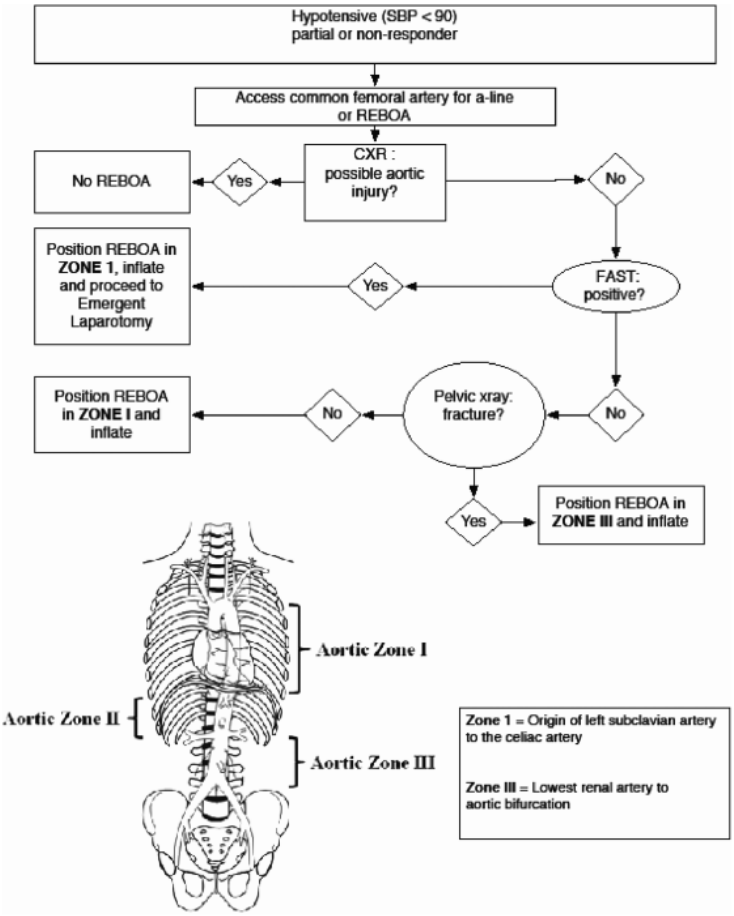
(Complete) A VIST simulator training program with powerpoint lectures and hands-on training was established. A description of the indications for REBOA is given, as well as a detailed description of step-by-step method of performing REBOA. After the lecture, participants were then trained and allowed to practice the individual steps of performing REBOA on a VIST Mentice simulator (Mentice, Gothenberg, Sweden).

Task 2: Standardize clinical performance of REBOA using simulator and formalized SOP (2-5 m).

2a. Standardize clinical performance of REBOA on simulator. (2-4 m).

2b. Formalize standard operating procedures. *Milestones: Formal SOP written. (2-5m).*

2a/b.(Complete) Clinical performance of REBOA on the VIST Mentice simulator was standardized, as well as formal clinical standard operating procedure (see figure below).



Task 3: Evaluate 30 physicians performance in REBOA placement in humans. (3-12 m).

3a. Log simulator usage by each physician (3-12 m).

(Complete) Log simulator usage by each physician. This task is complete, 43 out of 30 physicians have had simulator usage logged as of 5/30/2016.

3b. Track physician performance in REBOA placement. (3-12 m).

(Incomplete) Track physician performance in REBOA placement. This task is ongoing.

3c. Interim analysis after first 15 physicians complete the course (12 m)

(Complete). Interim analysis after first 15 physicians complete the course was completed.

3d. Statistical Analysis. *Milestone: A validated REBOA placement training program (11-12 m).*

(Incomplete) Statistical analysis is ongoing.

Milestone: A validated REBOA placement training program. 90% complete

Finalization of hypothesis 1 is ongoing. An abstract of the findings was written and presented at the Annual Meeting of American College of Surgeons, October 16-20, 2016 (see abstract below—also cited as #17 in Appendix C). A manuscript is currently in process.

RESUSCITATIVE ENDOVASCULAR BALLOON OCCLUSION OF THE AORTA (REBOA) CAN BE DEPLOYED RAPIDLY AND SAFELY BY ACUTE CARE SURGEONS

DAVID HAMPTON MD, MENG, WILLIAM TEETER MD, GEORGE HAGEGEORGE, MELANIE HOEHN MD, DEBORAH STEIN MD, MPH, THOMAS SCALEA MD, MEGAN BRENNER MD, MS

Introduction: REBOA is an emergent procedure requiring endovascular skills. We hypothesized there was no difference in REBOA deployment times or complications between acute care surgeons (ACS) trained in endovascular procedures during residency (ACS-EP) and those who did not (ACS-NEP), and ACS virtual reality simulation (VRS) and clinical procedural times did not differ.

Methods: Patient demographics, vital signs, and trauma statistics were obtained. ACS professional training and surgical case history were documented. All ACS completed a 1-day REBOA VRS course. The procedural time was defined as the interval from common femoral arterial access to balloon inflation. Published VRS results were compared to clinical performance. Intra-group ACS and patient comparisons were made using chi squared and student t-tests. Significance was $p < 0.05$.

Results: Twenty-eight REBOAs were performed: ACS-EP (n=11) vs. ACS-NEP (n=17). There was no difference in admission SBP, HR, ISS, or BMI between patients treated by either group. There was no difference in intra-group procedure times (ACS-EP: 303 seconds (SD:±100) and ACS-NEP: 315 seconds (SD:±105), p=0.46). There was no difference in ACS REBOA procedure times as compared to VRS training (ACS: 310 seconds (SD:±102) versus VRS: 277 seconds (SD:±55), p=0.18). There were no REBOA-related complications. Sixty-eight percent of patients arrived in arrest, and 30-day survival was 11%.

Conclusion: There was no difference in REBOA deployment times or complications between the two groups. ACS-NEPs can perform REBOA rapidly and safely after completion of a 1-day VRS course. This is the first study to validate transfer of skills from VRS to clinical performance of REBOA.

Appendix C: Products

Manuscripts

DoD Combat Casualty Care Research Program 2016 Supplement to Journal of Shock

12. Resuscitative Balloon Occlusion of the Aorta: Pushing care forward
    Authorship: W Teeter MD, A Romagnoli MD, J Glaser MD, A Fisher PA, J Pasley DO, B Scheele DO, M Hoehn MD, M Brenner MD

Introduction: Resuscitative endovascular balloon occlusion of the aorta (REBOA), used to temporize non-compressible and junctional hemorrhage, may be deployable to the forward environment. Our hypothesis is that non-surgeon physicians and high-level military medical technicians are able to learn the theory and insertion of REBOA.

Methods: US Army Special Operations Command (USASOC) medical personnel without prior endovascular experience were included. All subjects received didactic instruction of the Basic Endovascular Skills for Trauma (BEST) Course™ together, with individual evaluation of technical skills. A pre-test and post-test was administered to assess comprehension.

Results: Four members of USASOC including two non-surgeon physicians, one physician assistant (PA), and one special operations combat medic (SOCM) were included. REBOA procedural times moving from Trial 1 to Trial 6 decreased significantly from 186±18.7 seconds to 83±10.3 seconds ($p < 0.0001$). All subjects demonstrated safe REBOA insertion and verbalized the indications for REBOA insertion and removal through all trials. All five procedural tasks were performed correctly by each subject. Comprehension and knowledge between the pre-test and post-test improved significantly from 67.6±7.3% to 81.3±8.1% ($p = 0.039$).

Conclusions: This study demonstrates that non-surgeon and non-physician providers can learn the steps required for REBOA after arterial access is established. While insertion is relatively straightforward, the inability to gain arterial access percutaneously is prohibitive in providers without a surgical skill-set, and should be the focus of further training.

Abstracts

1th Annual Academic Surgical Congress Abstract Submission - February 2-4, 2016 in Jacksonville, FL

13. Virtual Reality Simulation for Residents: A Trainee Experience in Damage Control Endovascular Skills
    Authorship: William A. Teeter, MD, MS; Megan Brenner, MD, MS; Melanie Hoehn, MD; Deborah Stein, MD, MPH; Thomas Scalea, MD

BACKGROUND: The use of catheter-based techniques is increasing in the field of trauma. Virtual reality simulation (VRS) is a well-established means of endovascular skills training, and other simulation skills are now mandatory for board-eligibility in general surgery. Training for emerging endovascular damage control skills in trauma, including resuscitative endovascular balloon occlusion of the aorta (REBOA), may be obtained by residents through VRS.

Methods: Fifteen trainees in either an ACGME-approved General Surgery or Surgical Critical Care Fellowship at one institution received didactic and instructional sessions on REBOA. The

subjects performed the procedure 6 times. Subjects were excluded if they had taken a similar endovascular training course, had post-graduate training in endovascular surgery, or had performed the procedure in the clinical setting. Performance metrics were measured on a Likert scale, and included procedural time; accurate placement of guide wire, sheath, and balloon; correct sequence of steps; economy of motion; and safe use of endovascular tools. A pre- and post-course test and questionnaire were completed by each subject.

Results: Fifteen subjects, with a mean PGY level of 4.9 years (SD±0.95) participated in the study. Significant improvements in knowledge ($p < 0.0001$, CI 95%), as assessed by a standardized exam, were observed at the completion of the course. Procedural task times significantly improved from a mean of 207 seconds (SD ± 19.9) to 107 seconds (SD ± 20.6)[($p < 0.0001$, CI 95%] (Fig 1). No correlation was observed with endovascular experience in residency, number of endoluminal catheters placed per week, or other parameters. All trainees strongly agreed that the course was beneficial, and the majority would recommend this training to other trainees.

Conclusion: Damage control endovascular skills can be effectively acquired using VRS. Significant improvements in procedural time and knowledge can be achieved regardless of previous endovascular experience or area of training. Novice interventionalists such as surgical trainees can add a specific skill set (REBOA) to their existing core competencies. Use of this procedure in the clinical setting will determine if VRS for REBOA training confers validation metrics such as transfer of skills.

39th Annual CONFERENCE ON SHOCK – June 11-14th, Austin, TX

14. REBOA IMPROVES MEAN BLOOD PRESSURE (MBP) AND SHOCK INDEX (SI) AS MEASURED BY CONTINUOUS VITAL SIGNS (CVS) EVEN IN PATIENTS ARRIVING IN ARREST

    Authorship: W Teeter MD, M Brenner MD, M Hoehn MD, P Hu PhD, S Yang PhD

INTRODUCTION: Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) has been shown in both translational research and several case series to be a potentially life-saving procedure.

METHODS: We recorded systolic (SBP) & diastolic (DBP) blood pressure, heart rate (HR), and end-tidal CO2 (EtCO2) values every 2 seconds before (Pre), and after (Post) aortic occlusion (AO). Mean arterial blood pressure (MBP), shock index (SI), and pulse pressure (PP) were calculated from these values. Patients were included if they arrived without or lost a pulse prior to undergoing to REBOA at the diaphragm (Zone 1) and at least 15 minutes of continuous vital sign (CVS) monitoring. AO time was recorded in the medical record or determined by real-time video monitoring.

RESULTS: 15 patients met inclusion criteria, arriving to the trauma center in arrest or arresting shortly after arrival. Mean age (±SD) was 41 (±18 years), mean injury severity score (ISS) was 35 (±15), 79% were male, 10 sustained blunt injuries, and 4 sustained penetrating injuries. Seven patients experienced return of spontaneous circulation (ROSC) following AO by REBOA. Early deaths included 11 patients who expired in the ED and 1 in the OR, all within 2 hours. Ten patients died from hemorrhagic shock and one from severe TBI. Two patients died in the ICU, both from multisystem organ failure. None of the patients surviving to the ICU died from hemorrhagic shock, with two patients surviving around 12 hours, and one patient surviving

almost 9 days. Significant improvements in CVS pre- vs. post-AO were detected at 5 minutes for MBP (55.7±36.3-87.7±51.4mmHg; p<0.005), SI (1.4±0.8-1.1±0.6; p<0.004), and EtCO2 (14.0±11.2-18.4±12.1mmHg; p<0.004). Improvement in SI was significant at 10 minutes (1.4±0.9-1.1±0.7; p<0.004), and EtCO2 was significantly improved at all intervals (p<0.004). Improvements approaching significance were seen in mean SI, SBP, MBP and EtCO2 over all intervals.

CONCLUSION: Improvements in SI, MBP, and EtCO2 occur after REBOA, even in patients without signs of life on arrival. CVS monitoring, along with video recording of the procedure to accurately record time of AO, provides reliable data in order to study the technique and physiologic consequences of REBOA

75th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery - September 14-17, 2016, Waikoloa, HI

15. Time to aortic occlusion: It's all about access

Authorship: A Romagnoli MD, W Teeter MD, J Pasley DO, P Hu PhD, G Hagegeorge, D Stein MD, T Scalea MD, M Brenner MD

Introduction: Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a less invasive method of proximal aortic occlusion compared to resuscitative thoracotomy with aortic cross-clamping (RTACC). The aim of this study was to compare time to aortic occlusion with REBOA and RTACC, both including and excluding time required for CFA cannulation.

Methods: Patients receiving REBOA or RTACC performed between Feb 2013 and Jan 2016 captured on real-time videography were included. Timing of all procedural steps was collected: initial skin incision to aortic cross-clamp for the RTACC group, time from guide-wire insertion to balloon inflation at Zone 1 (just above diaphragm) for the REBOA group, and length of time required for CFA cannulation prior to REBOA. Time to common femoral artery (CFA) cannulation for REBOA by percutaneous or open methods was also compared.

Results: During the study period, 18 RTACC and 21 REBOAs were performed. There was no significant difference in age or gender between the two groups. There was no significant difference in procedure times between the 8 clamshell and 10 left side-only thoracotomies (376±188s vs. 361±144s; p = 0.85). Mean time from initial skin incision to aortic cross clamping in the RTACC group was 370±165 seconds, while mean time from start of arterial access to Zone 1 balloon occlusion was 492+/-107s (vs. RTACC, p=0.0084). All REBOA procedures were performed with the same device which requires a guidewire platform and large arterial sheath. The mean time to complete CFA cannulation was 252+/-112s, with no difference between percutaneous or open procedures access (p = 0.74). The mean time to aortic occlusion in REBOA once arterial access had been established was 240+/- 81s, which was significantly shorter than RTACC (p = 0.0031). There was no difference in mortality between RTACC and REBOA. Trainees performed the procedures in 3 cases (14%) for REBOA and 2 cases (11%) for RTACC.

Conclusions: Time to aortic occlusion, once CFA is achieved, is faster with REBOA, emphasizing the importance of rapid and accurate CFA access. Time to aortic occlusion is also less than the time required to cannulate the CFA either by percutaneous or open approaches. REBOA may represent a feasible alternative to thoracotomy for aortic occlusion in the hands of physicians who are highly skilled at arterial access procedures. Time to aortic occlusion once CFA is achieved will likely decrease with the advent of newer technology that eliminates the

need for a long guidewire platform. The rate-limiting and longest portion of the REBOA will continue to be obtaining CFA access.

75th Annual Meeting of AAST and Clinical Congress of Acute Care Surgery - September 14-17, 2016, Waikoloa, HI

16. Age is just a number: REBOA can be performed in older patients at high risk for atherosclerotic vascular disease
    Authorship: M Ghneim MD, W Teeter MD, A Romagnoli MD, M Hoehn MD, P Hu PhD, T Scalea MD, M Brenner MD

Background: With the advent of REBOA utilization as a means of proximal aortic control for end-stage hemorrhagic shock and the aging trauma population, comes the question of feasibility and efficacy of REBOA in the patient population with age-related vascular disease. The objective of this report was to describe technical success in REBOA placement in this patient population at high-risk for atherosclerotic disease.

Methods: Retrospective data was collected for patients ≥ 55 years of age who underwent REBOA between February 2013 and October 2015 at an urban tertiary care facility. Demographics and pertinent medical and surgical history were collected. Systolic blood pressure (SBP) measurements were obtained pre- and post- aortic occlusion. Procedural characteristics were obtained by videography, and signs of atherosclerotic vascular disease were obtained from CT imaging and autopsy reports.

Results: REBOA was performed in 15 patients older than 55 years of age, all who sustained blunt injury. Average patient age was 65±9 (range: 55-81) years, ISS 31±13 and base deficit of 5±9. After REBOA placement, computed tomography of the abdomen and pelvis with contrast was performed in 8 patients and autopsies in a further 2 patients, which revealed non-circumferential calcifications within the aortoiliac system and bilateral common femoral arteries. No patient had a prior aorto-, iliac-, or femoral vascular reconstruction. Nine patients were undergoing cardiopulmonary resuscitation (CPR) upon admission. REBOA was inserted with technical success in Zone 1 (just above the diaphragm) in 9 cases, and in Zone 3 (infrarenal aorta) in 6 patients. Arterial access was accomplished via direct cut down (n=4), percutaneously (n=9) or percutaneous converted to a cut down due to inability to access the artery in two patients with ongoing CPR. Mean SBP over the 15 minutes prior to REBOA was 62.5±13.7mmHg, with improvement to a mean of 95.5±31.7mmHg ($p < 0.001$) after aortic occlusion. PRBC 6.6±6.5, FFP 3.5±4 and Platelets 1±1.3. Overall mortality was 67%. Two Zone 1 patients survived to undergo surgical exploration, but Zone 1 in-hospital mortality was 100% and average survival time was 34.2 minutes (5-117). Four Zone 3 patients underwent embolization and surgical intervention and Zone 3 in-hospital mortality was 17%. Time to occlusion when compared to a concurrently enrolled younger patient population was similar (7.7min vs. 9min; $p = 0.2$). There were no procedural complications.

Conclusion: REBOA appears to be safe and effective in patients with mild to moderate atherosclerotic disease presenting with end-stage hemorrhagic shock and/or arrest based on lack of procedural complications and significant increases in systolic blood pressure post aortic occlusion. These results suggest that age does not appear to be a contraindication to REBOA.

American College of Surgeons Clinical Congress 2016 - October 16–20, 2016, Washington, DC.

17. Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) Can Be Deployed Rapidly and Safely by Acute Care Surgeons
    Authorship: D HAMPTON MD, W TEETER MD, G HAGEGEORGE, M HOEHN MD, D STEIN MD, T SCALEA MD, M BRENNER MD

Introduction: REBOA is an emergent procedure requiring endovascular skills. We hypothesized there was no difference in REBOA deployment times or complications between acute care surgeons (ACS) trained in endovascular procedures during residency (ACS-EP) and those who were not (ACS-NEP), and their procedural times did not differ between virtual reality simulation (VRS) and clinical performance.

Methods: Patient demographics, vital signs, and trauma and mortality statistics were obtained. ACS professional training and practice demographics were documented. The ACS-EPs performed more than 25 endovascular cases during residency training; the ACS-NEPs performed zero. All ACS completed a 1-day REBOA course, and the published VRS results were compared to clinical performance times. The procedural time was defined as the interval from successful common femoral arterial access to balloon inflation as seen on time-stamped video recordings of the
resuscitations.

Results: Twenty eight REBOAs were performed: 11 by ACS-EP and 17 by ACS-NEP. ACS-EPs (n=5) practiced significantly fewer years than ACS-NEPs (n=4); median 4 vs 17 years ($p<0.01$). There was no difference in admission SBP, HR, ISS, or BMI between patients treated by either group. Arterial access via open groin exposure was used more frequently in the ACS-EP group, 90% vs 47% ($p=0.04$). Aortic balloon occlusion was performed in Zone I (n=19) and Zone III (n=9). There was no difference in REBOA procedure times (ACS-EP: 303 seconds (SD:100) and ACS-NEP: 315 seconds (SD:105), $p=0.46$). There was no difference in REBOA procedure times as compared to VRS training (ACS: 310 seconds (SD: 102) and VRS: 277 seconds (SD: 55), $p=0.18$). There were no REBOA-related complications. 68% of patients arrived in arrest, and 30-day survival was 11%.

Conclusion: Even though well-established surgeons may not have trained in a technologically advanced environment as compared to more recent general surgery graduates, there was no difference in REBOA deployment times or complications between the two groups. ACS without extended formal training in endovascular procedures can perform REBOA rapidly and safely after completion of a 1-day course. This is the first study to validate transfer of skills from VRS to clinical performance of REBOA.

American College of Surgeons Clinical Congress 2016 - October 16–20, 2016, Washington, DC.

18. Paradigm shift in hemorrhagic traumatic arrest: REBOA is at least as effective as RTACC
    Authorship: W Teeter MD, A Romagnoli MD, H Li PhD, S Yang PhD, P Hu PhD, D Stein MD, T Scalea MD, M Brenner MD

Introduction: Resuscitative endovascular balloon occlusion of the aorta (REBOA) is a less invasive method of aortic occlusion in traumatic arrest as compared to resuscitative thoracotomy with aortic cross-clamping (RTACC). The aim was to compare short-term outcomes of patients receiving REBOA or RTACC.

Methods: Patients with traumatic arrest at a tertiary trauma center who had REBOA between 2013 and 2015 and patients between 2008 and 2013 receiving RTACC were included. Continuous recorded vital signs for all patients were prospectively collected.

Results: 19 RTACCs and 17 REBOAs were performed during the study periods. Most patients were male, mean age was 37±15 vs 41±16 years for RTACC vs REBOA. Median ISS was 31[18, 58] vs 26[19, 34], respectively (p=0.19). All patients were in arrest or arrested shortly after arrival. Mean admission SBP between groups was: RTACC 28±50mmHg vs REBOA 14±34mmHg (p=0.3). Median admission GCS was 3 in both groups: representing 75% of RTACC and 90% of REBOA. Similar rates of return of spontaneous circulation [7 (36.8%) RTACC vs 9 (52.9%) REBOA patients (p=0.5)] and patients surviving to OR [13 (68.42%) vs. 9 (52.94%), (p=0.49)] were seen. Mean SBP following aortic occlusion was slightly higher in REBOA (RTACC 46±39 vs REBOA 80±55 mmHg, p=0.13). Survival was not significantly different between groups: all but 1 patient died, the sole survivor (REBOA) was discharged to home.

Conclusions: REBOA may be an acceptable alternative to thoracotomy in traumatic arrest patients. Short term outcomes were no different between groups, but a trend toward a higher SBP after aortic occlusion was demonstrated with REBOA.

American College of Emergency Physicians Annual Meeting 2016, October 15-20th, 2016, Las Vegas, Nevada.

19. REBOA improves quality of resuscitation versus thoracotomy in patients in traumatic arrest.

    Authorship: William Teeter, MD MS, Anna Romagnoli, MD,, Melanie Hoehn, MD, Jay Menaker, MD, Deborah Stein, MD MPH, Thomas Scalea MD, Megan Brenner MD MS.

Introduction:
Resuscitative endovascular balloon occlusion of the aorta (REBOA) is emerging as a potential alternative to resuscitative thoracotomy (RT) in select patients with exsanguinating hemorrhage below the diaphragm. For those patients in cardiac arrest, the combination of aortic occlusion and cardiac massage, either via closed chest compressions (CCC) or open chest cardiac massage (OCCM), may increase cerebral and coronary perfusion, as well as decrease distal hemorrhage. The purpose of this study is to compare the quality of CCC or OCCM that patients receive in REBOA versus RT.

Methods:
From May 2014 to April 2016, any patient arriving in traumatic arrest and receiving aortic occlusion with REBOA or RT were included. All patients were in arrest on, or shortly after, arrival. Patients with cardiac injury requiring surgical intervention were excluded. Total Cardiac Compression Time (TCCT, minutes: seconds) is defined as the total time that CCC was performed for REBOA patients, and the total time that CCC (prior to RT) and OCCM (after chest opened) was performed for RT patients. All resuscitations were captured by prospective, real-time, multi-view videography. Exact times for all steps in the resuscitation were reviewed and documented by two independent physician reviewers. Statistical tests used include t-test for continuous data, and Fischer's exact test for categorical data.

Results:
During the study period, 47 patients with aortic occlusion after arrest were enrolled: 19 REBOA and 28 RT. Most were male (89%). Mean age was 35±14 years and mean ISS was 29.5±20.3

neither of which differed between groups (ISS all $p > 0.5$). The mean time of TCCT for each group was 15:44±07:20 for REBOA vs. 11:08±07:41 for RT. As a percentage of the total length of resuscitation, TCCT for REBOA was significantly improved over RT (84.9±13.2% vs. 54.5±18.7%, $p < 0.0001$). Resuscitation as measured by TCCT improved for RT after open cross-clamp to 67.6±25.8% of the time, but remained significantly less than the same period for REBOA 86.9±11.1% ($p = 0.004$). The difference in TCCT occurring prior to aortic occlusion by either REBOA or open cross-clamp was even more pronounced, with compressions occurring 88.3±7.8% of the time during resuscitation with REBOA vs 35.4±16.6% of the time in patients receiving RT.

Conclusion:
REBOA is currently being performed as an alternative to RT in select centers for patients with exsanguinating hemorrhage below the diaphragm, including those in arrest. This shift in practice decreases the morbidity of aortic occlusion, decreases the exposure hazard for providers, and may improve resuscitation. These results suggest that the length of cardiac compressions is longer for patients receiving REBOA versus RT before, during, and after aortic occlusion. A published multi-institutional trial has demonstrated that the time from admission to aortic occlusion is similar between the two procedures. The time required to perform the thoracotomy for RT may be better spent performing CCC concurrently with REBOA, as that lost time significantly reduces length of time of cardiac compression, and possibly cerebral and coronary perfusion. Variables for perfusion during resuscitation must be examined in order to understand the effects of cardiac compressions and aortic occlusion on patients in arrest due to hemorrhagic shock.

American College of Emergency Physicians Annual Meeting 2016, October 15-20th, 2016, Las Vegas, Nevada.

20. Virtual Reality Simulation can help prepare Emergency Medicine physicians for REBOA
    Authorship: W. Teeter MD, A Romagnoli MD, M Hoehn MD, J Menaker MD, D Stein MD, T Scalea MD, M Brenner MD

BACKGROUND:
Resuscitative endovascular balloon occlusion of the aorta (REBOA) is emerging as a bridge to hemostasis in patients with exsanguinating hemorrhage below the diaphragm, as well as a means to increase cerebral and coronary perfusion in patients arriving in arrest. This procedure is currently used in a small number of tertiary trauma centers by Acute Care Surgeons (ACS) in the United States, and internationally by Emergency Medicine (EM) providers both in the ED and in the field. Virtual Reality Simulation (VRS) is a well-established means of endovascular skills training for REBOA. We hypothesize that EM providers can learn the concepts and skill required for REBOA using VRS.

Methods:

EM trainees in ACGME-approved Critical Care Fellowships at one institution received didactic and instructional sessions on REBOA. The subjects performed the procedure 6 times. Subjects were excluded if they had taken a similar endovascular training course or had performed the procedure in the clinical setting. Performance metrics were measured on a Likert scale, and included procedural time; accurate placement of guide wire, sheath, and balloon; correct sequence of steps; economy of motion; and safe use of endovascular tools. A pre- and post-course test and questionnaire were completed by each subject. Analysis included simple linear regression and the Student's t test. A p-value below 0.05 was considered statistically significant.

Results

Ten subjects, with a mean PGY level of 4.6 years (SD±0.5) participated in the study. No correlation with task times was observed with any confounder studied including previous endovascular training or experience, number of central and arterial lines placed recently, or number of intra-aortic balloon pumps placed in training. Procedural task times improved from a mean of 218±19 to 106±15 seconds with a mean difference of 112 seconds, indicating the task time improvement from Trial 1 to Trial 6 was significantly different from 0 ($p < 0.001$). There was significant improvement in comprehension and knowledge between the pre-test and post-test, as their average performance improved from 74.3 ± 13.6% to 96.4 ± 5.0% ($p<0.001$).

Conclusion:

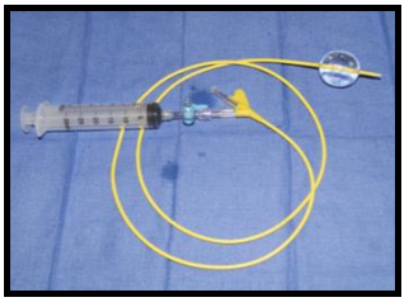
Significant improvements in procedural time and knowledge can be achieved by EM physicians based on VRS. Advances in technology will decrease the tools and steps required for REBOA, and ultimately decrease the time to occlusion for all providers. Despite these encouraging results and regardless of advances in equipment, successful REBOA utilization will be contingent on patient selection and common femoral artery access which may not be possible without operative exposure. These areas should become a focus of further training.

REBOA for Severe Pelvic Fracture and Intra-abdominal Hemorrhagic Shock

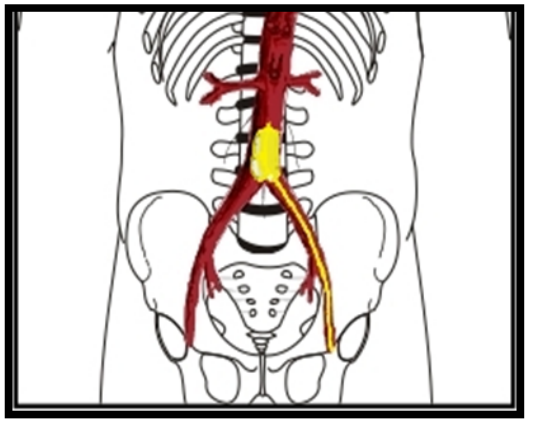
Log No. 13057166
W81XWH-15-1-0025

PI: Megan Brenner M.D. **Org: University of Maryland, Baltimore Award Amount: $999,999**

•**Problem:** Pelvic fracture with shock represents a common form of non-compressible torso hemorrhage on the battlefield. Currently there are few rapidly deployable, hemorrhage control and resuscitative procedures for this complex injury pattern.
Military Relevance: Military research has identified high potential for Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) as a rapidly deployable adjunct to control hemorrhage and improve central aortic pressures in this stetting.[1] Clinical study of REBOA for complex pelvic fracture and shock in the civilian setting has not been performed but stands to translate to military patterns of injury.
• **Hypothesis:** Clinical use of REBOA with a commercially available balloon occlusion catheter can be and is safe and feasible using endovascular simulator to enhance skills and standardized operating procedures. Additionally application of REBOA results in reduced blood loss, improvement of central hemodynamics, fewer blood transfusion and less time to the operating room or interventional angiography suite.
•**Approach/ Study Aim:** Prospective observational trial of REBOA in level I civilian trauma center using commercially available devices



Coda® Balloon (Cook Medical, Indianapolis, IN)



[1]Morrison JJ, Percival TJ, Markov NP, Villamaria C, Spencer JR, Rasmussen TE. Aortic balloon occlusion is effective in controlling pelvic hemorrhage in porcine model. *J Surg Res* 2012; May 8

Timeline and Cost

Activities	CY 15	16		
REBOA skills training standardization				
Standardize clinical performance of REBOA using simulator				
Prospective Enrollment				
Clinical data analysis and interpretation				
Estimated Budget ($999,999)	**$544,233**	**$455,776**		

Updated: (Garza, Marcos 15Mar16)

Goals/Milestones
CY15 Goal – System demonstration
☑ Standardized protocol for REBOA placement (1-2 m)
☑ VIST simulator training program curriculum (0-3 m)
☑ Enroll 30 subjects in simulator curriculum: 26/30 (86% complete)
☑ Milestone: UMD and DOD IRB Approval (0-4 m)
☑ Retrospective Data Collection (33 of 30 estimated subjects enrolled)
☑ Train clinical staff (3-12 M)
☑ Develop Study database (3-6 M)
☐ Prospectively enroll 24 patients (5-12 m)
19 patients enrolled thru 02/29/2016

Budget Expenditure to Date
Projected Expenditure: $999,999
Actual Expenditure: $517,394.15

Appendix D: Quad Chart

Appendix E: University of Maryland IRB Modification approval letter (10/28/2015)

University of Maryland, Baltimore
Institutional Review Board (IRB)
Phone: (410) 706-5037
Fax: (410) 706-4189
Email: hrpo@som.umaryland.edu

APPROVAL OF RESEARCH NOTIFICATION

Date: October 28, 2015

To: Megan Brenner
RE: HM-HP-00061192-1
Protocol Version and ID #: N/A
Type of Submission: Modification
Type of IRB Review: Expedited
Modification request dated: 10/14/2015

Modification Approval Date: 10/28/2015
Approval for this project is valid until 5/25/2016

This is to certify that the University of Maryland, Baltimore (UMB) Institutional Review Board (IRB) approved the above referenced modification request for the protocol entitled, "*Clinical Study of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) for Severe Pelvic Fracture and Intra-abdominal Hemorrhagic Shock using Continuous Vital Signs* ".

The IRB approved this modification via expedited review pursuant to Federal regulations 45 CFR 46.110(b)(2)/21 CFR 56.110(b)(2).

The IRB made the following determinations regarding this submission:
- A waiver of consent has been approved per 45 CFR 46.116(d).
- A waiver of HIPAA authorization for release of the PHI identified in the CICERO application has been reviewed and approved for this research study.

Below is a list of the documents attached to your application that have been approved:
Eligibility Checklist for HP-00061192 v3-24-2015-1427219238785
bibliography
R. Jenkins HIPAA 201
C. Feather HIPAA 201.pdf
R. Jenkins HIPAA 125
J. Kidd HIPAA 125
10-14-15 REBOA data collection tool Revised.docx
J. Kidd HIPAA 201
K. Volpini CITI Completion Certificate
M. Scarboro CITI Completion Certificate
C. Feather HIPAA 125.pdf
K. Fioretti HIPAA 125
A. Romagnoli HIPAA 125_pdf.mht
A. Romagnoli HIPAA 201_pdf.mht
M. Scarboro HIPAA 201
K. Fioretti HIPAA 201
C. Feather CITI Completion Certificate

In conducting this research you are required to follow the requirements listed in the INVESTIGATOR MANUAL. Investigators are reminded that the IRB must be notified of any changes in the study. In addition, the PI is responsible for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.103(4)(iii)). The PI must also inform the IRB of any new and significant information that may impact a research participants' safety or willingness to continue in the study and any unanticipated problems involving risks to participants or others.

Research activity in which the VA Maryland Healthcare System (VAMHCS) is a recruitment site or in which VA resources (i.e., space, equipment, personnel, funding, data) are otherwise involved, must also be approved by the VAMHCS Research and Development Committee prior to initiation at the VAMHCS. Contact the VA Research Office at 410-605-7000 ext. 6568 for assistance.

The UMB IRB is organized and operated according to guidelines of the International Council on Harmonization, the United States Office for Human Research Protections and the United States Code of Federal Regulations and operates under Federal Wide Assurance No. FWA00007145.

If you have any questions about this review or questions, concerns, and/or suggestions regarding the Human Research Protection Program (HRPP), please do not hesitate to contact the Human Research Protections Office (HRPO) at (410) 706-5037 or HRPO@som.umaryland.edu.